

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 40564	FOR FURTHER ACTION See Form PCT/IPEA/416	
International application No. PCT/FI2003/000946	International filing date (day/month/year) 11.12.2003	Priority date (day/month/year) 11.12.2002
International Patent Classification (IPC) or national classification and IPC C12Q 1/68 // C07K 14/72		
Applicant Oy Jurilab Ltd et al		

1.	This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2.	This REPORT consists of a total of <u>7</u> sheets, including this cover sheet.
3.	This report is also accompanied by ANNEXES, comprising: <div style="margin-left: 20px;"> a. <input checked="" type="checkbox"/> (sent to the applicant and to the International Bureau) a total of <u>1</u> sheets, as follows: <div style="margin-left: 20px;"> <input checked="" type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions). <div style="margin-left: 20px;"> <input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box. </div> </div> </div> <div style="margin-left: 20px;"> b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions). </div>
4.	This report contains indications relating to the following items: <div style="margin-left: 20px;"> <input checked="" type="checkbox"/> Box No. I Basis of the report <div style="margin-left: 20px;"> <input checked="" type="checkbox"/> Box No. II Priority <div style="margin-left: 20px;"> <input checked="" type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability <div style="margin-left: 20px;"> <input type="checkbox"/> Box No. IV Lack of unity of invention <div style="margin-left: 20px;"> <input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement <div style="margin-left: 20px;"> <input type="checkbox"/> Box No. VI Certain documents cited <div style="margin-left: 20px;"> <input type="checkbox"/> Box No. VII Certain defects in the international application <div style="margin-left: 20px;"> <input type="checkbox"/> Box No. VIII Certain observations on the international application </div> </div> </div> </div> </div> </div> </div> </div>

Date of submission of the demand 08.07.2004	Date of completion of this report 27.01.2005
Name and mailing address of the IPEA/SE Patent- och registreringsverket Box 5055 S-102 42 STOCKHOLM Facsimile No. +46 8 667 72 88	Authorized officer Terese Persson/EÖ Telephone No. +46 8 782 25 00

Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of:

- ☐ international search (under Rules 12.3 and 23.1(b))
☐ publication of the international application (under Rule 12.4)
☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☐ the international application as originally filed/furnished

☒ the description:

pages 1-21 _____ as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☒ the claims:

pages 22-24 _____ as originally filed/furnished

pages* _____ as amended (together with any statement) under Article 19

pages* 25 _____ received by this Authority on 08.11.2004

pages* _____ received by this Authority on _____

☐ the drawings:

pages _____ as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☒ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing (*specify*): _____

☐ any table(s) related to the sequence listing (*specify*): _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing (*specify*): _____

☐ any table(s) related to the sequence listing (*specify*): _____

* If item 4 applies, some or all of those sheets may be marked "superseded."

Supplemental Box Relating to Sequence Listing

Continuation of Box No. 1, item 2:

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis of:
- a. type of material
- ☒ a sequence listing
- ☐ table(s) related to the sequence listing
- b. format of material
- ☒ in written format
- ☒ in computer readable form
- c. time of filing/furnishing
- ☒ contained in the international application as filed
- ☒ filed together with the international application in computer readable form
- ☐ furnished subsequently to this Authority for the purposes of search and/or examination
- ☐ received by this Authority as an amendment* on _____
2. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

* If item 4 in Box No. 1 applies, the listing and/or table(s) related thereto, which form part of the basis of the report, may be marked "superseded."

Box No. II Priority

1. ☐ This report has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested:
- ☐ copy of the earlier application whose priority has been claimed (Rule 66.7(a)).
- ☐ translation of the earlier application whose priority has been claimed (Rule 66.7(b)).
2. ☐ This report has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rule 64.1). Thus for the purposes of this report, the international filing date indicated above is considered to be the relevant date.
3. Additional observations, if necessary:

The priority is considered valid. Therefore, documents 'Clinical Autonomic Research, Volume 13, 2003, Gerasimos P. Sykiotis et al, "The alpha2B adrenergic receptor deletion/insertion polymorphism in morbid obesity", pages 203-207' and 'International Journal of Obesity, Volume 27, 2003, Suppl. 1, Siitonen N. et al, "The Association of Polymorphism in the alpha2B-Adrenergic Receptor Gene with type 2 Diabetes and Obesity", Column T2:P2-017' are not included in the statement in Box V.

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 22-26

because:

☒ the said international application, or the said claims Nos. 22-26
relate to the following subject matter which does not require an international preliminary examination (*specify*):

See PCT Rule 67.1.(iv): Methods for treatment of the human or animal body by surgery or therapy, as well as diagnostic methods.

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. _____
are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. _____ are so inadequately supported
by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 22-26

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

☐

has not been furnished

☐

does not comply with the standard

the computer readable form

☐

has not been furnished

☐

does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in the Annex C-bis of the Administrative Instructions.

☐ See Supplemental Box for further details.

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	<u>1-21, 27-29</u>	YES
	Claims		NO
Inventive step (IS)	Claims	<u>1-21, 27-29</u>	YES
	Claims		NO
Industrial applicability (IA)	Claims	<u>1-21, 27-29</u>	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

Documents cited in the International Search Report:

D1: WO 02066617 A2

D2: The Journal of Clinical Endocrinology & Metabolism, Volume 84, 1999, No. 7, Paula Heinonen et al, "Identification of a Three-Amino Acid Deletion in the alpha 2B - Adrenergic Receptor That Is Associated with Reduced Basal Metabolic Rate in Obese Subjects", pages 2429-2433

D3: International Journal of Obesity, Volume 25, 2001, K. Sivenius et al, "Effect of a three-amino acid deletion in the alpha2B-adrenergic receptor gene on long-term body weight change in Finnish non-diabetic and type 2 diabetic subjects", pages 1609-1614

D4: US 2002058618 A1

D5: US 6150389 A

D6: Annu. Rev. Pharmacol. Toxicol., Volume 32, 1993, Robert R. Ruffolo et al, "Pharmacologic and therapeutic applications of alpha2-adrenoceptor subtypes", pages 243-79

D1 discloses a method for detecting a risk of hypertension by determining the pattern of alleles encoding a variant alpha2B-adrenoceptor wherein the presence of the deletion/deletion (D/D) genotype indicates an increased risk for hypertension. D1 also discloses a kit comprising means for determining the pattern of alleles encoding a variants alpha2B-adrenoceptor in a sample. (Claims.)

D2 describes the effect of a polymorphism in the alpha2B-adrenoceptor on metabolic rate in obese subjects. In addition, correlations to heart rate, systolic blood pressure and obesity are also discussed. (Abstract; page 2430, column 2, paragraph 7-page 2431, column 1, paragraph 1; page 2432, column 1, paragraph 1.)

.../...

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of: BOX V

D3 has investigated the effect of an alpha2B-adrenoceptor polymorphism on body weight. It was shown that the genotype of two short alleles (Glu9/Glu9) was associated with an increase in body weight among non-diabetic subjects. (Abstract.)

D4 disclose the fact that subjects with a D/D genotype of the alpha2B-adrenoceptor gene have a significantly elevated risk for acute myocardial infarction. (Page 1, paragraph 8.)

D7 has investigated the association of a deletion/insertion polymorphism in the alpha2B-adrenoceptor with the basal metabolic rate and metabolic syndrome-related parameters of morbidly obese patients. However, no statically significant differences were detected.

D5-D6 is considered to disclose the general state of the art.

To summaries, the subject matter claimed in claims 1-21 and 27-29 is novel. The subject matter claimed in claims 1-21 and 27-29 is considered to involve an inventive step and is considered to be industrially applicable.

or tissue norepinephrine or epinephrine concentrations and/or antagonizing α_B adrenoceptors of the human subject or animal.

10/538198
JC17 Rec'd PCT/PTO 09 JUN 2005

24. The method according to claim 23, wherein said compound is a subtype
5 of a selective or nonselective α_{2B} -adrenoceptor antagonist.

25. The method according to claim 23 or 24, wherein said method is a gene therapy or gene transfer method.

26. The method according to claim 25, wherein the gene to be transferred is a non-variant α_{2B} -adrenoceptor gene or a fragment or derivative thereof.

10 27. Use of a kit for the detection of a risk of diabetes or a metabolic syndrome in a subject, the kit comprising means for determining the pattern of alleles encoding a variant α_{2B} -adrenoceptor in a biological sample taken from said subject, and optionally computer software to interpret the results of the determination.

28. The use according to claim 27, wherein said kit is used for determining
15 the presence or absence of a variant genotype of the human α_{2B} -adrenoceptor in said biological sample.

29. The use according to claim 27 or 28, wherein said kit comprises a capturing nucleic acid probe or an antibody.